WOMEN IN NEURO CONFERENCE

EST. 2024

Celebrating Women in Neuroscience

2024 WOMEN IN NEURO CONFERENCE ABSTRACT BOOKLET

Queen's UNIVERSITY

Thank you to our donors!

TABLE OF CONTENTS

Schedule at a Glance

8:30 AM – 9:00 AM	**Attendee Check-In** *DDQIC Rose Event Commons*
9:00 AM – 9:15 AM	**Opening Remarks** *DDQIC Rose Event Commons*
9:15 AM – 10:00 AM	**Keynote Address** – Dr. Sari van Anders *DDQIC Rose Event Commons*
10:00 AM – 10:15 AM	Break
10:15 AM – 11:45 AM	**Industry & Academia Panel** *DDQIC Rose Event Commons*
12:00 PM - 1:00 PM	LUNCH *LinQ Lab*
12:30PM - 2:30PM	**Headshots** *Mitchell Hall Foyer*
1:00PM - 2:00PM	**Poster Presentations: Odd Numbers** *DDQIC Rose Event Commons*
2:00 PM – 3:00 PM	**Poster Presentations: Even Numbers** *DDQIC Rose Event Commons*
3:00PM - 3:15PM	Poster Teardown & Break
3:15 PM – 4:15 PM	**Talk Session 1** *DDQIC Rose Event Commons*
3:15 PM – 3:30 PM *3:30 PM – 3: 45 PM* *3:45 PM – 4:00 PM* *4:00 PM – 4:15 PM*	Heidi Riek Eve Racette Stephanie Hobbs Raven Wallace
4:15 PM – 4:30 PM	Break
4:15 PM – 4:30 PM	**Talk Session 2** *DDQIC Rose Event Commons*
4:30 PM – 4:45 PM *4:45 PM- 5:00 PM* *5:00 PM – 5:15 PM* *5:15 PM – 5:30 PM*	Brenna MacAulay Shima Hassanpour Nethmi Illamperuma Emily Robichaud
5:30 PM – 5:45 PM	**Best Poster/Talk Awards & Closing Remarks** *DDQIC Rose Event Commons*

Talk Schedule

3:15 PM – 4:15 PM	**Talk Session 1**
3:15 PM – 3:30 PM	**Exploring oculomotor biomarkers for neurodegenerative disease diagnosis and features using structured and unstructured eye movement tasks** *Heidi Riek, PhD Candidate, Queen's University*
3:30 PM – 3: 45 PM	**Relevance of sex as a biological variable in assessing the efficacy of a gene replacement therapy for a mouse model of XLID98** *Eve Racette, PhD Candidate, Queen's University*
3:45 PM – 4:00 PM	**The impact of a murine coronavirus upon alpha-synuclein pathology in neurons and microglia** *Stephanie Hobbs, MSc Candidate, Carleton University*
4:00 PM – 4:15 PM	**The Dynamic Synchronization of Brain and Thought** *Raven Wallace, MSc Candidate, Queen's University*
4:30 PM – 5:30 PM	**Talk Session 2**
430 PM – 4:45 PM	**Bridging the gap: ghrelin and the effects of social stress on male and female mice** *Brenna MacAulay, PhD Candidate, Carleton University*
4: 45 PM- 5:00 PM	**Analyzing the Relationship Between Altered Descending Pain Regulation in Fibromyalgia Syndrome (FM) and its Connection to Autonomic Dysregulation: A Comprehensive Structural and Physiological Modeling (SAPM) Study Using Functional MRI Data** *Shima Hassanpour. PhD Candidate, Queen's University*
5:00 PM – 5:15 PM	**Timing of eye and hand movements during reaching depends on functional demands of gaze** *Nethmi Illamperuma, 3rd Year Undergrad, Queen's University*
5:15 PM – 5:30 PM	**Hydrogen peroxide and phosphotyrosine modulate voltage-dependent cation channels** *Emily Robichaud, MSc Candidate, Queen's University*

Speakers

Keynote Speaker: ***Dr. Sari van Anders***

Topic: *Feminist and Queer Neuroscience!*

Abstract: Feminist and queer approaches are vibrant and important for understanding the world, including in academic research. How might they connect to neuroscience? In this talk, Dr. van Anders will discuss feminist and queer neuroscience: what it is, what principles underlie it, and why it is valuable. To do so, Dr. van Anders will draw on her research in feminist/queer science, including theory and empirical work from social neuroendocrinology, gender/sex, and sexual diversity. She will articulate how feminist and queer perspectives help us move towards a neuroscience that is more empirical, accurate, and just.

Academia & Industry Panelists

Dr. Janis Kan

Bio: Dr. Janis Kan is a co-founder of Dynamiris and a postdoctoral fellow at the Centre for Neuroscience Studies at Queen's University (Kingston). Dynamiris is developing an objective and easy-to-use tool to aid in assessing neurological disorders, such as Parkinson's Disease, using non-invasive, video-based eye-tracking. She holds a PhD in Neuroscience from Queen's University and has over 15 years of experience using eye-movements and neurophysiology to study the brain, specializing in the brain circuitry that combines sensory and cognitive signals to drive eye-movements.

Dr. Karys Peterson-Katz

Bio: Dr. Karys Peterson-Katz is a post-doctoral research fellow with Infant and Early Mental Health Promotion, a program of the Hospital for Sick Children in Toronto. She received her Bachelors of Arts and Science (Honours) from McGill University, and her doctorate in Neuroscience from Queen's University. Her doctoral research focused on early childhood development across child welfare and community-based settings in Canada, and the implementation of developmental screening tools. She currently leads the work on the first Canadian database of development from infancy to age six.

Dr. Effie Pereira

Bio: Dr. Effie Pereira's research investigates the temporal dynamics of human attention, which primarily concerns how our attentional processes fluctuate over time. These fluctuations give rise to seemingly random variations in behaviour, which can often be quite predictable and structured. Over the years, she has used computational approaches with behavioural, eye tracking, EEG, and fMRI methods to study temporal dynamics when attending to social contexts, internal contexts, and digital contexts.

Dr. Michele Morningstar

Bio: Dr. Michele Morningstar's research focuses on the development of emotional communication and social cognition from childhood to adulthood. She is particularly interested in the ways in which we learn to express and perceive emotional states through nonverbal cues, such as tone of voice. She uses a variety of methods, including speech analysis and functional neuroimaging, to determine how these basic emotional skills contribute to our social functioning and psychological well-being across development.

Graduate Student Poster Abstracts

1. **Cellular Fate, Inflammation and Tissue Integrity in the Ischemic Cortex Following Middle Cerebral Artery Occlusion in Rats** *presented by Golnar Taheri, Queen's University*

Stroke is the third leading cause of mortality worldwide. The most common type of stroke is ischemic stroke, caused by impaired blood flow in the brain. Diffusion-weighted imaging (DWI) MRI is a sensitive method to detect cerebral ischemic changes, revealing acute ischemia as areas of restricted diffusion. Brain regions with DWI restriction have been associated with completed stroke in the ischemic core, representing areas with irreversible cellular death. However, rat and human studies have demonstrated partial and complete reversibility in these areas following the restoration of blood flow. These reversible areas represent tissues adjacent to the ischemic core and are of interest in stroke recovery because of their essential role in brain reorganization and behavioural recovery. The fate of the cells in these regions and the role of inflammation are yet to be characterized. By characterizing regions of DWI restriction reversal in the rat brain cortex using a tMCAO model, we aim to test two potential hypotheses: (1) CNS cells are differentially affected during acute and subacute phases of ischemia, and (2) some neuronal populations might exhibit increased resilience to ischemia by expressing proteins associated with neuroprotective mechanisms. The tMCAO model allows occlusion and reperfusion within the MRI to monitor ischemic tissue evolution and DWI-restriction reversal in a rat model. Using 2,3,5-triphenyl tetrazolium staining, regions of tissue death will be spatially registered to DWI images to confirm the cellular death within the DWI-restricted region and verify tissue viability in regions of DWI-restriction reversal. Coronal brain sections will be stained for neuronal marker NeuN, astrocyte marker GFAP, microglia marker Iba1, macrophage marker CD163 and endothelium marker CD31, which will be spatially registered on MRI images to provide an overlay to extract quantitative cell counts.

2. **Neuromelanin Alterations Associated with Problematic Social Media Use** *presented by Holly Shannon, Carleton University*

Background: Neuromelanin-sensitive MRI (NM-MRI) has demonstrated its potential as a proxy measure of dopamine functioning in the substantia nigra (SN). Elevated neuromelanin signal intensity has been associated with more severe substance use and sensitivity to social reward. Structural alterations in the reward system have been found with problematic social media use, however dopamine functioning has yet to be explored. The current study aims to determine whether higher problematic social media use is linked to altered neuromelanin signal intensity in the substantia nigra. **Methods**. Thirty-one young adults (18-35 years of age) completed the Bergen Social Media Addiction Scale to measure problematic social media use and underwent a NM-MRI scan. The contrast-to-noise ratio was calculated for each participant and at each voxel within the substantia nigra. Voxelwise analysis was performed to determine if problematic social media use was correlated with a significant number of voxels in the SN. Additionally, the average change in NM-MRI signal intensity was correlated with problematic social media use scores. Age was included as a covariate in both models. **Results**. Voxelwise analysis within the bilateral substantia nigra revealed 113 significant voxels with higher NM-signal intensity correlated to increased problematic social media use ($p < .05$ FDR). However, higher levels of problematic

social media use were not significantly associated with the average neuromelanin signal intensity across the substantia nigra (p = 0.30). **Conclusions**. These findings suggest a nuanced relationship between problematic social media use and neuromelanin intensity in the substantia nigra. Further exploration is warranted to uncover mechanisms underlying problematic social media use, to develop a more comprehensive understanding.

3. **Delivery of scAAV9-coGM2A for Phenotypic Correction of GM2 Gangliosidosis AB-Variant, in the Newly Characterized Gm2a/Neu3 Double Knockout Mouse Model** *presented by Camilyn Cheng, Queen's University*

GM2 Gangliosidoses AB-Variant (ABGM2) is an autosomal recessive lysosomal lipid storage disorder characterized by an overaccumulation of GM2 gangliosides in neuronal lysosomes, ultimately resulting in neuronal cell death. This disorder arises due to a mutation in the *GM2A* gene, which encodes for GM2 Activator Protein (GM2AP), an essential cofactor in the hydrolysis of GM2 gangliosides. Overaccumulation of GM2 gangliosides and eventual neuronal cell death present as phenotypic symptoms of sensory, motor, and cognitive decline and ultimately result in a shortened lifespan. In its most severe and common 'infantile' form, death can occur as early as 4 years of age. Currently, there are no curative treatments available for ABGM2; however the delivery of a gene therapy using an Adeno-Associated Virus expressing a codon-optimized *GM2A* transgene holds great promise to treat ABGM2. This study aims to investigate the dose-response of intrathecal delivery of scAAV9.co*GM2A* in the newly characterized *Gm2a*$^{-/-}$*/Neu3*$^{-/-}$ murine models for the first time. 5 cohorts each containing 6 mice received intrathecal administration at 6 weeks of age of either vehicle, or three different doses of vector per mouse – low (0.5e^{11}vg), medium (1.0e^{11}vg) or high (2.0e^{11}vg). Monthly behavioural testing and blood collections were performed starting at 8-weeks of age and were continued until either short-term endpoint of 27-weeks of age, or humane endpoint. At each respective endpoint, serum, gross organs and tissues from the central nervous system were collected for biochemical analysis of GM2 ganglioside accumulation, GM2AP activity, vector biodistribution, immune response and histology. Data will be shown to support the hypothesis that there will be a dose-dependent response in GM2 ganglioside accumulation, GM2AP activity, vector biodistribution to the central nervous system and improvement in behavioural outcomes in short-term and added survival benefits in long-term. Furthermore, immune responses will be tested through immunological assays. These results will provide more clinically translatable results on the efficacy and safety of scAAV9.co*GM2A* in treatment of ABGM2.

4. **Imaging-Based Analysis of Cerebrovascular Reactivity in Military Snipers Experiencing Repetitive Subconcussive Impacts** *presented by Kim Huynh, Queen's University*

Background. A subconcussive injury occurs from a direct or indirect impact to the head that does not result in overt symptoms. However, there is growing evidence that an accumulation of these subconcussive injuries can result in neurological symptoms including headaches, short-term memory problems, and sleep disturbances. Previous work done in our lab with magnetic resonance imaging (MRI) revealed that football athletes who experienced a greater number of subconcussive impacts had elevated cerebrovascular reactivity (CVR). CVR reflects the ability of the cerebral blood vessels to dilate in response to an increased demand for blood. We have partnered with the Canadian Special Operations Forces Command to study subconcussive injury in their personnel. Military snipers are continually exposed to subconcussive impacts as the stock of their weapon impacts the shoulder and transfers recoil forces to the head.

Anecdotally, some snipers report either constant neurological symptoms after an accumulation of high caliber rifle recoil forces throughout their careers or a decreased threshold for symptoms as their careers progress. **Methods.** In the current study, 15 military snipers (37±6 years) were recruited to assess changes in CVR following a sniper training course involving repetitive subconcussive impacts. All participants received an MRI scan before (PRE) and after (POST) a sniper training course. The MRI protocol included a BOLD sequence where participants were connected to the RespirAct gas control system (Thornhill Medical, Toronto, Canada). FSL was used to process the data and CVR was calculated using the seeVR toolbox.A paired sample t-test was conducted to compare PRE and POST differences in CVR maps using FSL's *randomise*. **Results**. There was a significant increase in CVR (P<0.1) in the right frontal medial cortex. These findings suggest that repetitive subconcussive impacts may cause local increases in CVR, emphasizing the importance of incorporating additional cerebrovascular metrics when analyzing neurophysiological changes after subconcussive impacts.

5. **Exploring the Feasibility and Efficacy of a 12-Week, Psilocybin-Assisted Online Cognitive Behaviour Therapy Program for Women with Perimenopausal Anxiety** ***presented by Sandy Luu, Queen's University***

Background. During perimenopause, women may develop anxiety, which can be challenging to treat with traditional medication and hormone treatments. A novel strategy for addressing anxiety during perimenopause is psychedelic therapy, particularly with psilocybin. Psilocybin is a compound naturally present in psychedelic mushrooms that can alleviate anxiety symptoms. As such, psilocybin treatment can benefit women with perimenopausal anxiety. When paired with psychotherapy, clients can make the most of both treatments. Cognitive Behavioral Therapy (CBT) is one of the leading therapies for anxiety disorders and can be delivered fully online (e-CBT) to offer accessibility and convenience. **Aims and Hypothesis.** We will examine the practicality and usefulness of a program designed for women with perimenopausal anxiety that combines psilocybin and e-CBT. We predict that psilocybin will boost treatment results and improve symptoms of generalized anxiety. We will also examine other perimenopausal symptoms as exploratory outcomes. **Methods.** We will offer mid-aged women with perimenopausal anxiety a 12-week, psilocybin-assisted e-CBT program where they will receive controlled daily doses of psilocybin, complete at-home e-CBT modules, and receive feedback on e-CBT homework through a secure platform. We will also use validated mental and menopausal health questionnaires to determine program efficacy and to evaluate symptoms at the start of the study, after 6 weeks, and at the end of the 12 weeks. **Significance.** No studies have explored whether it is possible and effective to combine psilocybin treatment with e-CBT, let alone to treat perimenopausal anxiety. This trial will add to the field of reproductive health and psychedelic therapy while inspiring innovative approaches to treating anxiety disorders.

6. **A Neurocomputational Model of Negative Emotions In Dietary Control** ***presented by Tavneen Sandhu, Queen's University***

Many people struggle to adopt and maintain healthy diets to combat excess weight gain. Yet an escalating global epidemic of obesity is taking over many parts of the world. For example, 26.8% of Canadian adults are categorized as obese, and 36.3% are overweight, yielding increased health risks like cancers or cardiovascular diseases. One factor contributing to dietary control failures is the role of negative emotions and people's inability to cope with their affective states by using high-caloric foods as a means of emotional comfort. The impact of negative

emotions on behaviours can be exacerbated by being hungry (colloquially referred to as "hangry," a combination of angry and hungry). Our study investigates the neurobiological basis and impact of "hangriness" on dietary success and the mitigating role of a person's ability to regulate emotions (which differs dramatically across people). Participants will attend two laboratory sessions, hungry (after 6 hours of fasting) vs. satiated (after a meal), while they perform an established food choice task, and their brain responses are measured via electroencephalogram recordings. In both sessions, participants will also encounter a frustration task to evoke negative emotions ("hangriness") and sustain these emotions throughout the session. Brain data will allow examining how negative emotions alter activation in the brain's decision network, yielding more unhealthy dietary patterns in the food task. Established self-report measures of people's emotion regulation abilities will enable testing of how this capacity can "protect" healthy diets. Our results might help develop novel interventions to manage emotional eating effectively and inform stakeholders in public health, educational institutions, and individuals who struggle with dietary control in the face of negative emotions (especially when hungry).

7. **Drawing improves memory in a free recall task and evokes unique thought patterns to promote successful memory** ***presented by Silvia Zhou, Queen's University***

For millennia, humans have created drawings as a means of externalizing visual representations, and later, to aid communication and learning. Despite its cultural value, we understand little about the cognitive states elicited by drawing, and their downstream benefits. In two preregistered experiments, we explored these states; Undergraduate participants (*N*s = 69, 60) encoded words by drawing or writing, periodically describing their thoughts using multi-dimensional experience sampling, a tool for characterizing the features of ongoing thought. Subsequent memory was tested via free recall. Contrasted with writing, drawing improved memory, and evoked thoughts that were more visual and elaborative. Recall was also dictated by the emergence of these thought patterns, with the former most important when drawing. Our findings establish that drawing elicits unique thought patterns that promote successful memory, providing an explanation for drawing's influential role in our everyday lives.

8. **Correction of Arginine:glycine Amidinotransferase (AGAT) Creatine Deficiency through a Novel Bicistronic AAV9 Construct** ***presented by Tesla Peretti, Queen's University***

Creatine is a small molecule that plays an important role in energy metabolism and is required for overall health and neurodevelopment as seen from creatine deficiency disorders (CDD). CDDs are inborn errors of metabolism which result in neurological manifestations including intellectual disability, developmental delay, and seizures emphasizing the importance of creatine in brain function. Endogenous production of creatine begins through the enzymatic function of arginine:glycine amidinotransferase (AGAT) to form guanidinoacetate (GAA) which is then converted to creatine by guanidinoacetate methyltransferase (GAMT) enzyme. AGAT-deficiency (AGAT-D) is an autosomal recessive disorder caused by loss of function mutations in the *GATM* gene encoding the AGAT protein preventing endogenous creatine production. Currently, the only treatment for AGAT-D relies on daily creatine supplementation, however this is not curative and does not restore AGAT function or appropriate creatine levels in the brain, leaving many symptoms untreated. We have performed a proof-of-concept *in vitro* study using two plasmid constructs- *phGATM* and *phGATM-GAMT*, through transfecting AGAT knockout HAP1 cells. Results demonstrate restoration of AGAT protein and creatine production. HAP1

cells were cultured in specialized media so that any creatine quantified would have to be produced by the cells. The cell lysates were analyzed for guanidino compounds such as creatine and GAA through liquid chromatography tandem mass spectrometry. Both constructs were able to restore creatine production, however in the *phGATM* treated cells, GAA levels were significantly elevated which could lead to potential neurotoxic effects likely due to relative GAMT-D, while the *phGATM-GAMT* treated cells received both enzymes for the pathway preventing GAA accumulation. These results have inspired the *in vivo* proof-of-concept study that is currently underway using *AAV9.hGATM* and *AAV9.hGATM-GAMT* vectors in murine models of AGAT-D. Further studies will aid in determining optimal efficacy and safety of the vectors for translation into clinical use for AGAT-D and potentially other diseases.

9. **Focused Ultrasound & Microbubbles Induced Blood-Brain Barrier Opening and Alteration Of Brain Metastases Microenvironment** ***presented by Dure Khan, Queen's University***

Brain tumours are hard to treat due to the presence of Blood-Brain Barrier (BBB) limiting the passage of drugs into the parenchyma. Focused Ultrasound (FUS) stimulated Microbubbles (MBs) are a non-invasive, image-guided technology allowing for safe, transient disruption of the BBB. While preclinical studies have showed alterations in cytokines and chemokines of healthy brain post-sonication with MBs, elucidating the effects of FUS & MBs on tumour microenvironment (TME) is needed. This study aims to characterize the cytokine and chemokine profiles of breast-cancer metastases in the brain post-sonication with MBs. It is hypothesized that pro-inflammatory cytokines will be detected in higher concentrations in tumour versus healthy brain tissue post-FUS&MB treatment. 30,000 human metastatic MDA-MB-231 breast cancer cells were directly injected into the right frontal lobe of immunocompromised mice via a burr-hole. Tumour growth was monitored by MRI, and mice were treated with FUS&MBs when tumours reached a diameter of 3-5mm. Pre-and post-treatment MRI scans were obtained to visualize the BBB-opening, validated with intravenous injections of 2% Evans Blue as well as by analysing the relative change in contrast enhancement. Mice were euthanized 1-hour post-treatment and fresh and frozen samples were collected for analyses. Preliminary results from female mice (n=4) suggest Eotaxin, G-CSF, IL-9 and IL-12p70 levels were significantly increased ($p<0.05$) in tumour vs healthy samples. Further analysis reveals upregulation of proinflammatory cytokines and chemokines in the FUS & MBs treated tumour samples in comparison to non-treated tumours. This study will improve understanding of tumour and TME alterations following FUS&MB treatment and guide future therapies for brain tumour patients.

10. **Age Related Changes in Neural Markers of Real-World Social Functioning** ***presented by Sarah Saju, Queen's University***

It is an extremely common truism that humans are social creatures and as social species, humans are continuously required to process various complex social signals in order to form and maintain relationships. It is also true that there is variation in individual capability to form said relationships with some thriving in their social lives while others struggle to maintain a few connections. It therefore brings to question if there are particular neurobiological mechanisms behind why some people are more well integrated in social networks while others are not. This becomes an important topic to explore knowing that deficiencies in social relationships are associated with an increased risk of developing multiple diseases, having negative impacts on

mental and physical health. Furthermore, the prevalence of social isolation and loneliness, particularly after the pandemic and in the aging population, make clear that these are major public health and social issues. This study, using a fMRI social information processing task (EmpaToM), aims to provide insight into the precise mental and neural mechanisms explaining why some people struggle making and sustaining social connections and relationships by (1) seeing if activation in specific neural networks can be predictive of individual social network size and (2) examining age-related changes in the ability to maintain large social networks and its association with neurobiological changes. Observing brain activity together with computational models and machine learning techniques will allow us to examine the link between neural substrates and real-world social functioning. Ultimately, these findings may aid healthcare practices, policymakers, and stakeholders in addressing significant health, social, and economic changes in the coming decades in the face of aging societies worldwide.

11. How We Learn to Optimize Blink Timing in Structured Tasks ***presented by Isabell Pitigoi, Queen's University***

Spontaneous blinking of the eyes is an essential physiological behaviour famously responsible for lubricating the cornea and protecting the eye from foreign particles. However, humans blink at a much higher rate than necessary for these purposes alone, suggesting that higher level cognitive, social, or environmental factors may be involved. It has been shown that blinks occur at implicit breakpoints in a task and are sensitive to internal mental states related to attention and cognitive demand. Here, we aim to characterize eye blink behaviour in healthy individuals performing a structured interleaved pro- and anti-saccade task (IPAST). Data was collected from 608 controls spanning the ages of 5-93 years (390 female, 218 male) and analyzed to understand blink timing in relation to task demands. Blinks were highly organized, occurring most often at times when visual attention was less critical to performance and cognitive load was lower. For example, participants suppressed eye blinks more often on anti-saccade trials (which are more difficult to perform than pro-saccade trials). These patterns emerged and strengthened overtime, changing most rapidly throughout the first 40 trials, suggesting that the timing structure is quickly learned. At reproductive age, females had a higher blink rate than males overall, and higher blink probability during fixation, pointing to potential social or hormonal interactions in blink circuitry. These findings represent a fundamental understanding of blink behaviour under different task conditions and describe variability between sexes and across lifespan. This is crucial for the discovery of non-invasive ocular markers of cognition, memory, and motor decline, which would have profound implications for earlier diagnosis and intervention in many neurodegenerative or psychiatric patient groups.

12. The psychological and biological toll of burnout and chronic stress in healthcare workers: Study Protocol ***presented by Chelsea Montgomery, Carleton University***

Background: Burnout, an occupational stress syndrome, is characterized by emotional exhaustion, depersonalization, and decreased professional accomplishment. As of Spring 2021, more than half of healthcare workers (HCWs) in Canada report severe burnout, which coincides with higher rates of depression, anxiety, and trauma. However, burnout and its impact are still not fully understood. Thus, this interdisciplinary study aims to assess biological and psychological changes associated with burnout and chronic stress among HCWs. **Methods:** Multi-modal neuroimaging and blood and saliva samples will be used to assess the relationships among burnout, stress and changes in brain structure and function, epigenetics, immune and

stress activation, and levels of growth factors, in a cohort of 100 licensed HCWs working at Ottawa-area hospitals. Participants will complete online self-report questionnaires to assess demographic information, psychosocial measures, such as burnout, stress and moral distress, mental health symptoms, and mental health service use at baseline, six months and one year following their in-person study visit. **Progress and Hypotheses:** This study has enrolled 50 participants (41 F, 9 M). We expect participants who report higher burnout symptoms and moral distress will also report higher anxiety, depression and trauma symptoms. Burnout is expected to be associated with higher inflammation, decreased levels of cortisol and growth factors, reduced hippocampal and amygdala volume, decreased activation of frontolimbic brain regions, and altered methylation of stress-related genes. This data will be integrated into a machine learning algorithm, to identify risk and resilience to burnout in healthcare. **Significance:** Combining results from neuroimaging with peripheral markers of stress and inflammation will provide a well-rounded understanding of the biological impact of burnout and chronic stress among HCWs, as well as further our understanding of burnout. Results from this study can help inform tailored treatment strategies and interventions to support HCWs.

13. Dose Response of Dual Route *scAAV9-HEXM* Gene Transfer in a Mouse Model of Sandhoff Disease *presented by Brianna Quinville, Queen's University*

Sandhoff disease (SD) is caused by the excessive accumulation of GM2 gangliosides in the lysosomes of neuronal cells. Typically, these lipids are hydrolyzed by an enzyme, β-hexosaminidase A (Hex-A), a heterodimer comprised of an α- and a β-subunit. Mutations in the gene encoding either subunit can lead to improper functioning of the enzyme. SD is caused by a mutation in the *HEXB* gene resulting in a deficient or absent β-subunit and subsequent accumulation of GM2 gangliosides. This causes widespread cell death, and consequently progressive symptoms and rapid neurological decline culminating in death by age 4 in the most prevalent, infantile form of the disease. A homodimer formed by a novel hybrid μ-subunit called HexM, an isoenzyme of human Hex-A, has been recently developed and shown to hydrolyze GM2 gangliosides *in vivo*. Previous studies have determined the effectiveness of gene transfer with the gene, *HEXM,* packaged in a self-complementary adeno-associated viral vector, serotype 9 (scAAV9), through increased life span in a SD mouse model (*Hexb*$^{(-/-)}$). This study aims to determine the dose response of the *scAAV9-HEXM* treatment in the SD mouse model through dual delivery of treatment via intra-cisterna magna (ICM) and intravenous (IV) routes, along with the ancillary administration of immunosuppressant drugs. Treatment for 10 cohorts of 10 mice involved concurrent infusions through both ICM and IV routes. There were three possible infusates for the ICM route (vehicle, low or high vector dose) and six possible infusates (vehicle, 5 different vector doses) for the IV route. The study design allows an efficacy comparison of the total dose when administered either through one route of delivery or split between the two. The researcher who conducted the procedure and subsequent testing is blinded to which dosage each animal received. Bimonthly behavioural testing and blood collections at specific time points were done until mice reach their humane endpoint as determined by specific UACC criteria. At termination, blood, gross organs, brain, and spinal cord were collected for analysis of GM2 ganglioside accumulation, vector copy number, Hex enzyme activity, cellular and humoral immune response, and histology. To date the results from the long-term study show increased survival in all treatment groups compared to the vehicle-only control group ($p < 0.001$ in all cases). The treatment cohort with the longest survival showed a >6.5-fold increase in median survival compared to the control group. Additionally, some treated cohorts showed a >3-fold

decrease in accumulated gangliosides compared to controls in the mid-section of the brain ($p < 0.01$). In sera collected at humane endpoints there was a >51-fold increase in Hex enzyme activity in the longest living treatment group compared to heterozygous controls ($p < 0.05$). Ganglioside accumulation in the cerebellum, Hex activity in the brain, vector biodistribution, and behavioural data will also be shown.

14. Delivery of scAAV9.co*SLC6A8* for restoration of creatine transporter function in a creatine transporter deficient mouse model: a dosage study ***presented by Chiara Sawilla, Queen's University***

Creatine deficiency syndromes describes inborn errors of creatine metabolism, impairing affected individuals' synthesis and transport of creatine. One such disease is creatine transporter deficiency (CTD). CTD, an X-linked disorder, results from mutations in the *SLC6A8* gene and renders creatine transporters in affected patients dysfunctional. Under normal physiological conditions creatine is synthesized endogenously and released into the blood stream to provide cellular energy. Creatine uptake is reliant on Na^+/Cl^- dependent creatine transporters as they deliver the synthesized creatine against a large concentration gradient into cells. Mutations in *SLC6A8* present clinically as intellectual disability, developmental delays, behavioural abnormalities, and speech and motor impairments. There are currently no treatments for CTD; creatine supplementation has shown limited success in restoring creatine levels in the brain of those affected. Thus, therapies focus on behavioural and seizure management strategies. The delivery of a codon optimized *SLC6A8* transgene via self-complementary adeno-associated virus 9 (scAAV9.co*SLC6A8*) has been proposed as a treatment for CTD. Previously, delivery of *SLC6A8* transgene via intracerebroventricular injection at 1 day of age in a *Slc6a8*$^{Y/-}$ murine model showed increased creatine levels in the brain, a decrease in hyperactivity, and an increase in muscle strength. This study aims to investigate the dose-response of the scAAV9.co*SLC6A8* using intrathecal route in a *Slc6a8*$^{Y/-}$ murine model. 5 cohorts (n=6 mice) received either vehicle, low dose ($3.5e^{11}$ vg/mouse), medium dose ($7.5e^{11}$ vg/mouse), or high dose ($1.1e^{12}$ vg/mouse), as well as a daily administration of immunosuppression with rapamycin and prednisone beginning at 5 weeks of age and injections at 6 weeks of age. Both short term (13 weeks) and long term (24 weeks) cohorts undergo grip strength testing at 13 weeks. Long term cohorts will also undergo blood collection at 13 weeks, hyperactivity analysis in a digitally ventilated cage at 22-24 weeks, and a final grip strength test at 24 weeks. At the endpoint- serum, peripheral organs, and central organs will collected for biochemical analysis. Data will be shown for short-term and long-term analysis. Our hypothesis is that the medium and high dose cohorts will show greater levels of creatine in the central nervous system, greater grip strength, and less hyperactivity when compared to vehicle control groups. Results of this study will provide important information for a future clinical trial.

15. Understanding Stressful Experiences as a Risk Factor for Problematic Cannabis Use ***presented by Keira Aubin & Isabella Hotston, Carleton University***

The legalization of cannabis has been accompanied by a rise in problematic usage patterns among young adults, who are particularly vulnerable to its impacts. While early-life trauma (ELT) is a known predictor of problematic cannabis use, very little research explores neurobiological changes associated with this relationship. Recent interest in the regulatory involvement of the endocannabinoid system (ECS) in cannabis use, the stress response, mood disorders, addictions, and ELT aligns with investigating the relationship between ELT and problematic

cannabis use. The primary objective of this research is thus to identify a unique circulating endocannabinoid and diurnal cortisol profile that may explain the relationship between ELT and problematic cannabis use. This research also aims to identify how endocannabinoid levels may differ across a range of cannabis users, from non-users to recreational and chronic users. Finally, we also hope to understand how sex and gender may play a role in moderating these relationships. University students who do and do not use cannabis will be brought into the lab to complete a series of questionnaires assessing ELT, mental health, and cannabis use. We will also collect blood and saliva for later processing of diurnal salivary cortisol and plasma endocannabinoid analysis. The second phase of this study includes a similar survey to re-evaluate mental health and cannabis use after one year. Ultimately, this study will provide insight into key biomarkers associated with ELT, current stress, and problematic cannabis use. The exploration of the biological underpinnings of problematic cannabis use among young adults will not only facilitate more informed use within this population, but also holds the potential for informing targeted therapeutic interventions and clinical strategies.

16. Profiling CHIP to reveal genetic alterations associated with Alzheimer's Disease ***presented by Alexandra McDonald, Queen's University***

Collaborative biomedical research yields pathogenesis understanding and supports early detection strategies for age-related illnesses like Alzheimer's disease (AD). Curiously, immune system activation and successive recruitment of inflammatory cells has been shown to be both protective and harmful in AD pathology. This may be linked to the point in which immune system activation occurs in relation to the cell cycle, so warrants exploration. We use Clonal Hematopoiesis (CH), a condition involving pre-cancerous blood cells, to guide our exploration. AD and CH both involve inflammation and increased risk with age. CH is associated with a two-fold increase in cardiovascular risks and an inflammatory state linked to coronary artery disease, yet recent research suggests CH *protects* against AD. Building on these findings, our project aim is to expose future research and detection targets by investigating this surprising relationship. We have extracted Whole Genome Sequencing (WGS) data from the UK biobank, a large-scale biomedical database, to investigate the relationship between CH and genetic alterations found to be protective in AD pathology. We include genetic changes relevant to inflammation, and those associated with protection with or without known mechanisms. Integrating germline data will help characterize the role of acquired (somatic) mutations in blood cells- in AD pathology, including the downstream effects. This will inform the development of a targeted panel to use with cell free and genomic DNA in AD specific cohorts. Dr. Rauh, a hematologist and expert in CH, and Dr. Crocker, a cytogeneticist with expertise in constitutional and acquired genetic disorders and neurodegeneration, will co-supervise this project. The integration of cross disciplinary expertise with current research in both hematology and neuroscience provides the ideal context for a project that will return data in both spheres. Clarifying the relationship between CH and AD can elucidate detection and treatment targets and lays the foundation for early intervention.

17. Identifying Features of Glioblastoma Recurrence and Invasion ***presented by Kaytlin Andrews, Queen's University***

Glioblastoma (GB) is the most common malignant brain tumour. Unfortunately, despite some improvement in the 2-year survival rate, the long-term prognosis has not significantly improved for the past 40 years, with 5-year survival rate of around 5% and overall mortality close to 100%.

Even with maximal therapy, which includes surgery, radiation, and chemotherapy, the median overall survival is only 12-18 months. Patients who undergo gross total resection and who have tumor-free margins, have delayed time to recurrence and improved overall survival compared to those who undergo subtotal resection or a biopsy. There is specific function to every millimeter of brain and although we can resect some areas of the brain, it comes at cost to the patient. Furthermore, there are highly eloquent regions that cannot be disrupted even if therapeutically beneficial. Therefore, if we could identify which tissue outside of the tumour cavity is at highest risk of recurrence and which areas are at low risk of recurrence, we could then provide the benefits of supramarginal resection without the cost of unnecessary brain tissue resection. The goal of this project is to create a tool that allows us to acquire high-density, image-guided biopsies of the tumor cavity following gross total resection of a GB. These biopsies will enable us to describe the biochemical, molecular, and cellular features of the tumour niches that drive GB recurrence. We will then distill the high dimensional descriptive data we acquire into simple, cost-effective assays that allow for maximal resection of high-risk surrounding tissue and preservation of low-risk tissue. If successful, this would set the foundation for a personalized, precision approaches to both GB resection and/or post-operative radiation.

18. Alternative splicing acts as a method of regulating phosphorylation events in normal cerebellar development and sonic hedgehog subgroup medulloblastoma *presented by Kana Ogawa, Queen's University*

Phosphorylation is a ubiquitous post-translational mechanism that is critical in all aspects of cellular biology including development and cancer. It is orchestrated by protein kinases that phosphorylate a magnitude of substrates for malignant transformation. As these promiscuous effectors are nonspecific and reversible, they impose difficulties in targeting the function of a singular protein. Post-transcriptional regulation, such as alternative splicing (AS), generates diverse RNA and protein variants and may serve as a potential avenue to identify critical regulators of development and tumourigenesis. An illustrative model to understand this biological process is sonic hedgehog (SHH) subgroup medulloblastoma (MB), which arises from granule neuron precursors (GNPs). These GNPs, found abundantly in the cerebellum, are induced by SHH and can either differentiate into granule neurons or undergo transit amplification to form a MB. We have generated comprehensive GNP and MB time course datasets that provides us the opportunity to observe normal cerebellar development and MB progression in comparison. Our preliminary work indicated that AS may influence MB formation through selective inclusion or exclusion of exons containing vital phosphorylation sites ("phosphosites"). By identifying differential splice variants and their corresponding phosphosites that are critical to MB growth and determining their respective functional consequences of over- and under- expression, my research aims to unveil unconventional aspects of developmental regulation and establish a new governing process involved in tumour initiation, in which AS and phosphorylation together contribute to molecular control. This research proposal addresses a significant gap in our understanding of post- translational regulation in cancer formation, particularly in the context of MB, the most common pediatric brain tumour[6]. It aims to shed light on the complex interplay between AS and phosphorylation, providing insights into both normal developmental processes and the initiation of tumours. The findings from this study could have implications for cancer biology, potentially leading to innovative approaches for cancer treatment and therapeutic development.

19. Controlling Calcium Influx during Tonic Neuronal Activity *presented by Ariane Hadziomerovic, Queen's University*

Calcium (Ca^{2+}) is a molecule which helps regulate excitability, gene expression and secretion in neurons[1]. Multiple mechanisms are involved in getting Ca^{2+} into the cell through channels, as well as circulating it throughout specific organelles in the cell, which uptake and release Ca^{2+} when needed[2]. Importantly, Ca^{2+} in the cell leads to negative feedback on Ca^{2+} channels at the surface of the cell, temporarily blocking Ca^{2+} uptake through Calcium-Dependent Inactivation (CDI)[2]. Previous research has found that some of these mechanisms are more active during specific stages of neuronal signalling[2]. Much research has been done on which mechanisms are contributing during the fast-phase of neuronal signalling, which is categorized by -60mV firing at a frequency of 5Hz for 1 minute[3]. However, the majority of signalling is composed of the slow phase, which has -40mV 1Hz signalling lasting 30 minutes[3]. Despite knowing that Ca2+ levels stay stable during this tonic period, we have yet to undercover the complexities of the mechanisms involved to maintain Ca^{2+} levels consistent. Whole-cell voltage clamp recordings were taken from bag cells of *Aplysia californica*; these bag cells are neuroendocrine and induce ovulation through the secretion of hormones triggered by intracellular Ca^{2+} concentrations[3]. Preliminary findings show evidence that bag cell neurons experience a reversal of Ca^{2+} influx at around +50mV. It was also found that cells held at -40mV experienced a higher level of rundown compared to cells held at -60mV and -80mV. These findings suggest that there is a difference in how Ca^{2+} is cycled throughout the cell between fast-phase and slow-phase activity. Further research will be conducted to understand what Ca^{2+} cycling mechanisms are more present during tonic neural activity.

20. Individual variability in affective modulation of pain perception in brainstem and spinal cord regions identified using fMRI *presented by Hannan Algitami, Queen's University*

Pain perception involves both sensory and affective components, which both contribute to chronic pain conditions. Additionally, chronic pain conditions are often diagnosed alongside mood disorders, both of which involve persistent negative affect. Although it is known that negative affect and pain are connected, how they influence each other remains unclear. Hence, this study aimed to investigate the neural correlates of negative affect and how it influences pain perception. To do this, we analyzed brainstem and spinal cord fMRI data from a previous affective modulation study performed in our lab. During fMRI data acquisition, participants experienced a noxious heat stimulus on their right hand while viewing affective images from the International Affective Picture System (IAPS). We then used Structural and Physiological Modelling (SAPM) to analyze the data and extract information about excitatory and inhibitory connectivity between regions involved in pain processing. We compared negative and neutral affective conditions in terms of pain intensity and unpleasantness ratings, and corresponding connectivity values. We also identified two distinct neural connectivity "patterns" among the group of participants to identify differences in pain perception and connectivity that can be attributed to individual differences. The results showed that affective conditions and connectivity patterns varied significantly in terms of pain unpleasantness, but not intensity. Moreover, connectivity patterns differed more in terms of pain ratings and connectivity than affective conditions. These results illustrate that the effect of individual differences was greater than the affective modulation effect evoked by viewing the images.

21. Exploring Self-Stigma and Attitudes Towards Alcohol Abstinent Canadian Undergraduate Students *presented by Tanisse Teale, Carleton University*

Background: A trend of alcohol abstinence and reduced alcohol use among young adults has been identified among many countries, including Canada. Few studies have characterized the experiences of those who are alcohol abstinent, particularly in normative alcohol cultures such as universities. This study identifies differences between alcohol-abstinent and non-abstinent Canadian undergraduates, exploring predictive factors for self-stigma and negative attitudes towards those who are alcohol abstinent. **Methods:** Eighty-eight alcohol abstinent and 92 non-alcohol-abstinent Canadian undergraduates completed self-report questionnaires, including the UCLA Loneliness Scale, Motives for Abstaining from Alcohol Questionnaire, Self-Stigma and Alcohol Dependence Scale, and Regan's Attitude Towards Non-Drinkers Scale. **Results:** Students who do not drink alcohol exhibited greater loneliness (p = .02), reduced social connectedness (p = .03), and more unsupportive interactions with parents (p = .02). Those who are alcohol abstinent show increased self-stigma if they are not drinking alcohol out of fear-of-consequences (R^2 = 0.03, b = 0.16, t = 0.54, p = .59). Those who use alcohol displayed more negative attitudes towards those who do with increased alcohol use (R^2 = 0.23, b = 0.69, t = 5.14, p < .001). **Conclusions:** This study is one of the first to describe an understudied population; specifically, university students who are alcohol-abstinent, revealing the social challenges faced by those who do not drink alcohol. The impact of alcohol use on negative attitudes towards those who do not drink alcohol underscores the necessity of a comprehensive understanding of social dynamics in the context of alcohol abstinence among young adults.

22. Altered social behaviours in adolescence and adulthood in a rat model of early-life resource scarcity *presented by Megan Babcock, Queen's University*

In the limited bedding/nesting (LBN) paradigm dams are provided with insufficient bedding and nesting material, thus altering maternal care and, in turn, the neurodevelopmental trajectory of the offspring. In this study, 24 litters of Long-Evans rats were randomly assigned to either the Control or LBN condition, from postnatal day (PD) 2-9. LBN dams displayed higher levels of rough handling of pups (e.g., drag, step on) than controls, likely indexing greater stress. LBN offspring subsequently spent less time grooming the nape of a conspecific's neck in a standard social interaction test (SIT). Notably, this effect was apparent when LBN offspring were tested in either adolescence or adulthood. Since the nape is a primary playfighting target in rats, this suggests LBN alters this critical social behaviour. Ongoing work is assessing oxytocin mRNA expression in the paraventricular nucleus of these offspring. Although robust, levels of playfighting behaviour in that study were unusually low, thus limiting our ability to examine changes in other aspects of playfighting. This led to a follow-up study aimed at increasing baseline playfighting. A separate group of 24 male Long-Evans were tested in the SIT, in a 2 (Lighting: red light vs. darkness) x 3 (Social isolation: 0hr, 5hr, 24hr) design. Rats tested in darkness displayed higher rates of playfighting behaviours (i.e., nape attacks and pinning) compared to rats tested under red light. Rats isolated for 24-hours displayed greater playfighting behaviour than non-isolated rats. These follow-up findings suggest that rats' social play behaviour is ideally assessed in complete darkness after at least 24-hours of social isolation. Our revised protocol will allow us to better assess the impact of LBN on offspring social behaviour.

23. Improvements in anti-saccade performance in patients with major depressive disorder following repetitive transcranial magnetic stimulation of the dorsolateral prefrontal cortex *presented by Rachel Yep, Queen's University*

Repetitive transcranial magnetic stimulation (rTMS) of the dorsolateral prefrontal cortex (DLPFC) is an effective treatment for individuals with major depressive disorder (MDD) who do not respond to traditional interventions. However, the mechanisms by which mood symptoms improve with rTMS remain unclear. One possibility is that rTMS enhances cognitive control by modulating the central executive network. To test this hypothesis, we examined a well-characterized eye tracking task known to recruit the central executive network: the interleaved pro/anti-saccade task (IPAST). On pro-saccade trials, participants are required to look at a peripheral stimulus, yielding a measure of processing speed. On anti-saccade trials, participants are required to suppress the reflex to look at the stimulus and instead look away, yielding a measure of cognitive control. 29 patients with MDD (mean age=44.9 years, 48% female) completed the IPAST before and after 4 weeks of rTMS. 19 non-depressed control participants not undergoing rTMS (mean age=38.9 years, 58% female) completed the task at the same time points. Mixed ANOVAs were used to assess between- and within-group differences in pro- and anti-saccade reaction time (SRT). Pro-saccade SRT did not differ between groups ($F(1,46)=0.20$, $p=0.66$) or over time ($F(1,46)=0.64$, $p=0.43$), nor was there a significant group-by-time interaction. Anti-saccade SRT, however, was significantly longer in patients with MDD compared to controls ($F(1,46)=5.98$, $p=0.02$), and decreased significantly across participants over time ($F(1,46)=11.58$, $p=0.001$). The group-by-time interaction approached significance ($F(1,46)=2.36$, $p=0.13$), with anti-saccade SRT decreasing over time to a greater degree in patients with MDD compared to controls. These preliminary findings suggest a selective improvement in cognitive control in patients with MDD following rTMS of the left DLPFC. Future work will investigate task differences between patients who respond to rTMS versus those who do not.

24. Advanced neuroimaging modalities for improving epilepsy surgery assessment *presented by Andrea Ellsay, Queen's University*

Background: Around 30% of individuals with focal epilepsy are refractory to medical treatment, making neurosurgery a potential therapeutic option. However, identifying suitable candidates and localizing the epileptogenic zone remain challenging. We introduce three advanced neuroimaging techniques for pre-surgical assessment at the District Epilepsy Center, Kingston Health Sciences Center (KHSC). Additionally, we compare language lateralization results from different software tools to optimize language fMRI processing and analysis for clinical use. **Methods:** Patients in the pre-surgical pathway (n=21) underwent multidisciplinary team (MDT) discussions, excluding those with prior resections (n=5) or deemed unsuitable for surgery (n=4). Twelve patients with inconclusive clinical data underwent comprehensive MRI evaluation, including high-resolution 3D T1-weighted scans, 3D FLAIR, and fMRI for language lateralization. Language fMRI data was analyzed using (1) SPM12, (2) FSL and (3) fMRIPrep with SPM12. **Results:** Neuroimaging modalities significantly improved epileptic tissue localization, identified imaging abnormalities, and facilitated language lateralization. Following multimodal assessment, previously discussed surgery candidates were appropriately identified or advanced. Language lateralization indices showed concordance across software tools, except for four instances, suggesting similar performance despite language network reorganization in epilepsy patients. **Conclusions:** Considerations for software selection in epilepsy surgery

centers emphasize usability and institutional practices. These findings underscore the clinical value of advanced neuroimaging modalities and highlight the importance of standardized protocols and software considerations in epilepsy surgery assessment.

25. Changes in Social Environment Impact Primate Microbiome Composition *presented by Colleen Pearce, Queen's University*

Composed of trillions of microbes, the gut microbiome, also known as the "forgotten organ," is essential for health and wellbeing. Contemporary neurobiological studies underline its profound impact on cognition and behavior through the brain-gut-microbiome axis, with dysfunctions in this pathway having been linked to various health problems, including heart disease, cancer, and depression. Yet, the forces that ultimately shape the gut microbiome remain opaque. Perhaps the most poorly understood, yet potentially most consequential of forces that can shape the gut microbiome is one's social environment. Work in humans and nonhuman primates has suggested that cohabitation and frequent social interaction are responsible for similarities in gut microbiome composition. In turn, these studies have noted changes in behavioral and cognitive functioning as a result of these microbiota shifts. However, it is difficult to assess causation in these studies, and interpretations are complicated by the influence of uncontrolled but correlated factors known to directly impact the gut microbiome, such as diet. Here, we performed an investigation of the impact of changes in social environment on gut microbiome composition in a cohort of male cynomolgus macaques (Macaca fascicularis, ages 7 - 9yrs) while controlling for diet. Our longitudinal study design tracked 13 captive males through three 6-month phases of social living conditions (single housing to divided social living and back to single living) over an 18-month period, during which we collected feces and hair samples to assess changes in gut microbiome composition and systemic cortisol levels, respectively. We found that social living conditions significantly increased animals' cortisol levels, consistent with a physiological stress response associated with increased social interactions in males. Concomitant with these physiological effects, we also observed changes in gut microbiome composition above and beyond what could be explained by diet alone, indicating a direct effect of changes in social environment on gut biodiversity. Together, these findings suggest that changes in sociality can impact the physiology of primates at multiple biological levels, which may underlie the known relationship between social environment and individual wellbeing.

26. Investigating the Impact of Spatial Certainty and Target Features on Visual Search *presented by Hannah Lum Smith, Queen's University*

Searching for objects in scenes is influenced by a number of factors, including prior detailed knowledge about the target object and how it fits within the larger context. In this study, we varied the spatial certainty within the scene as well as the target template precision to examine whether search strategies differ qualitatively. Spatial Certainty (SC) of objects were rated independently according to whether they are associated with a single region (i.e., chandelier is high) or with multiple regions (i.e., cat is low). Participants searched scene images for 150 targets varying in SC and target templates were established with either a word or picture cue. Unexpectedly, although both higher Spatial Certainty and Picture Target Cues contributed to faster search, they did so independently. These findings suggest that influence of spatial certainty and target template may not be synergistic. We will explore this question further by examining eye movements.

27. Expression and function of guanidinoacetate methyltransferase (GAMT) is restored in cellular and murine models of GAMT creatine deficiency following treatment with *scAAV9.hGAMT* *presented by Robyn Binsfeld, Queen's University*

Creatine deficiency disorders such as guanidinoacetate methyltransferase deficiency (GAMT-D) are inborn errors of metabolism resulting in several neurological manifestations including developmental delay, intellectual disability, and epilepsy, emphasizing the role of creatine in the brain. Current treatments, while partially successful do not fully restore creatine levels or reduce accumulation of the toxic guanidinoacetate (GAA) intermediate in the brain. We present a proof-of concept study testing an AAV9-based gene therapy for treatment of GAMT-D. A construct containing the codon-optimized coding sequence for human *GAMT* was designed to be packaged in a self-complementary AAV9 vector. Plasmid DNA was delivered to knockout cells via lipid-mediated transfection and *scAAV9.hGAMT* via intrathecal lumbar puncture to GAMT-D mice. GAMT expression was assessed by western blot and qPCR, while tissues, and serum were analysed using mass spectrometry to detect creatine and GAA levels. Protein and mRNA expression of GAMT were restored resulting in increased intracellular creatine content and reduced GAA accumulation in cellular models of GAMT-D following treatment. In a murine model of GAMT-D, intrathecal delivery of *scAAV9.hGAMT*, significantly increased creatine content and decreased GAA accumulation throughout the body, including the brain. These same results were observed over time in the serum of treated animals compared to untreated controls. This study represents proof-of-principle results for effective restoration of GAA and creatine levels in the brain and periphery using an AAV9 based gene therapy. *scAAV9.hGAMT* is being further investigated to determine an appropriate therapeutic window for efficacy and safety with the goal of future translation to treat human patients.

28. Eye-tracking: a potential diagnostic tool for psychiatric disorders *presented by Blake Noyes, Queen's University*

Although numerous potential biomarkers for major depressive disorder (MDD) have been identified, there are yet to be any widely integrated into clinical practice (Strawbridge et al., 2017). In addition to inconsistencies within research, the invasiveness of traditional biomarker techniques, such as blood and genetic analysis, will pose challenges for clinical use. This problem may be addressed via eye tracking; a well-established, non-invasive technique to identify alterations in specific neural networks responsible for cognitive control, arousal, attention, and orienting responses. The goal of this ongoing study is to use video-based eye tracking to compare saccade behaviour, pupil size, and blink rate in people with MDD and healthy control subjects. The current sample includes 78 control subjects (mean age [M] 16.9 years, 59 female, Patient Health Questionnaire [PHQ] score = 2) recruited from the community and 26 adolescents with MDD (M = 15.9 years, 20 female, PHQ score = 14.3) recruited from a local psychiatric outpatient program. All participants completed self-report questionnaires for mental health symptoms and the Interleaved Pro-Anti Saccade eye-tracking task (Munoz et al., 2004). Preliminary analyses showed that participants with MDD had slower saccadic reaction time and generated more direction errors when making pro- and anti-saccades, blinked more during important visual instructions, and had blunted pupil responses throughout the task compared to control participants. Data collection is ongoing. These results suggest that eye tracking may be a feasible technique to distinguish people with MDD from control subjects and identify potential eye movement biomarkers for future diagnostic purposes.

Undergraduate Student Poster Abstracts

29. A Short Term Dosage Study Exploring A Gene Therapy For Guanidinoacetate Methyltransferase (GAMT) Creatine Deficiency *presented by Emahnee Cover, Queen's University*

Creatine is an essential amino acid required for energy metabolism, especially in tissues with increased energy requirements such as the brain. GAMT-D is a rare inherited metabolic disorder that affects the biosynthesis of creatine in the body. The lack of creatine production leads to various neurological symptoms ranging from intellectual disability, developmental delay and recurrent seizures. L-arginine:glycine amidinotransferase (AGAT) and Guanidinoacetate Methyltransferase (GAMT) are two enzymes in the creatine biosynthesis pathway that produce creatine from the initial precursors glycine and arginine. Individuals with GAMT-D exhibit a deficiency in the GAMT enzyme. In the absence of GAMT, the precursor Guanidinoacetate (GAA) cannot undergo conversion into creatine, leading to its accumulation and potential manifestation of neurotoxic effects. Gene therapy employing adeno-associated viral (AAV) vectors is a great candidate as treatment for GAMT deficiency due to its long lasting effects, low immunogenicity and ability to transduce several tissue types including the brain. In our research study we are evaluating the effectiveness of a monocistronic gene therapy in treating GAMT-D in a mouse model of the disease. By utilizing a self complementary AAV vector carrying the human GAMT gene, we can reinstate GAMT expression in order to decrease GAA accumulation and elevate creatine levels within the tissues particularly in the central nervous system. Previously we determined that a dose of 2.5e11 vector genomes per mouse was sufficient to increase creatine and decrease GAA levels significantly from untreated animals, however not completely to heterozygous levels. We are testing three doses categorized as high, medium, and low ranging from 1.3e12 to 2.5e11 vector genomes per mouse to determine the most efficient dose to restore creatine levels to that of heterozygous or wild type mice. Direct CNS administration will be employed through an intrathecal lumbar puncture injection at 6 weeks of age. Here we hope to present the outcome of this short-term high dose study as promising data for the use of this therapy in the treatment of GAMT-D. Ongoing studies continue to explore the efficacy and safety of this therapy for best translation into use in human patients.

30. Examining the impact of a double-hit model of depression-like behaviours in female Long-Evans rats *presented by Brando Sheldrick, Queen's University*

Early-life stress, including poverty, increases the risk of later life psychopathologies, such as depression. Due to ethical constraints, causal relations can only be investigated using animal models. The Limited Bedding and Nesting (LBN) paradigm is a naturalistic model of early-life resource scarcity where dams are supplied with restricted amounts of materials to build a nest. LBN alters maternal care behaviours which, in turn, negatively impacts offspring development. This study sought to examine a double-hit model of depression-like behaviour, whereby an environmental insult (i.e. LBN) during the animal's early life sensitizes them to a second "hit" of stress in adolescence, thus imparting greater depression-like behaviours relative to subjects who did not receive the double hit. On postnatal day (PD) 21, thirty-two female offspring consisting of

sixteen LBN and sixteen neonatal control (nCON) subjects were weaned into standard home cages, consisting of four rats of the same condition. All subjects were left undisturbed until PD48, after which half of the offspring from each neonatal condition were exposed to a subthreshold Chronic Mild Stress (CMS) paradigm, where they experienced two mild stressors (e.g., restraint stress; elevated platform exposure; food deprivation) each day, for a duration of 12 days. All subjects were then exposed to a forced-swim test in adulthood (>PD60). The only finding to emerge in that test was an increase in the latency to immobility displayed by the double-hit group relative to the single-hit groups and the control group. This might suggest higher levels of anxiety-like behaviour in rats exposed to both stressors. Current work is assessing oxytocin-producing cells in the paraventricular nuclei of all subjects using immunohistochemistry to investigate the effects at the neurological level.

31. Examining the association between exposure to major stressful life events and non-suicidal self-injury *presented by Cristina Misceo, Queen's University*

Experiencing major stressful life events (SLEs) may contribute to risk for non-suicidal self-injury (NSSI). Prior research has established that a higher number of SLEs is linked with more frequent NSSI episodes among young adults. However, life stress is typically assessed with checklist approaches; these methods introduce frequent idiosyncratic misinterpretations of stress categories (e.g., major illness). Coupled with the unclear boundary of what constitutes SLEs, relying on participants' subjective appraisals of stress severity attenuates validity. Specifically, individuals with a history of NSSI may have certain cognitive characteristics that contribute to an over-appraisal of event severity. Interview-based, contextual life stress systems overcome these limitations by having third-party raters blind to participant characteristics determine stress severity based on a standardized set of circumstances. Accordingly, this study used the Life Events and Difficulties Schedule 2 (LEDS-II), which is a gold-standard, semi-structured life stress interview and rating system. Specifically, we focused on the cumulative severity of episodic stressors (i.e., SLEs whose major features occur within a 2-week period). In our analysis of 101 participants (*M*age= 19.92, *SD*age= 2.59), cumulative stress severity (*M* =3.63, *SD* =3.00) was not significantly associated with the number of NSSI episodes participants reported in the past year (*M* = 19.31, *SD* = 54.90), $r(101) = .10$ $p = .314$. Current findings do not align with previous literature on the association between SLEs and NSSI. However, they provide a methodological foundation for how to improve future research on SLEs and NSSI in young adults through the application of gold-standard life stress measures.

32. Neuronal Integrity of Hippocampal Granule Cells in Primary Progressive Aphasia due to FTLD-tauopathies *presented by Vivienne Lubbat, Queen's University*

Primary progressive aphasia (PPA) is a dementia syndrome characterized by language impairment with memory sparing. PPA stems from underlying neuropathologies, including the tau form of frontotemporal lobar degeneration (FTLD-tau). Tau has different isoforms, with either 3 or 4 repeats in microtubule binding domains (3R or 4R). FTLD-tauopathies contain either 3R tau (Pick's Disease; PiD) or 4R tau (cortical basal degeneration, CBD; or progressive supranuclear palsy, PSP). Previous studies show that the dentate gyrus (DG) of the hippocampus is vulnerable to FTLD-tau inclusions, where PiD shows highest densities. The objective of this study was to examine neuronal size as a proxy for cellular integrity across FTLD-

tauopathies within the DG. This study included 25 participants with PPA diagnoses and autopsy-confirmed tauopathies. Paraffin sections of the left hippocampus were stained with 1.0% Cresyl Violet. Images were obtained at 20x and annotated. Average neuronal area (μm2) of neurons was calculated per group. Unpaired t-tests compared average neuronal area between 3R- and 4R tauopathies, and ANOVA compared average neuronal size between all three tauopathies. Pearson correlations calculated the relationship between neuronal size and tau-positive inclusion densities (count/mm3). Average neuron size was smaller in 4R tauopathies (M=91.69 μm2) compared to 3R tauopathies (M=103.3 μm2) ($p<0.05$). CBD showed smaller cells than PiD ($p<0.05$). Within 4R tauopathies, the significant negative correlation between neuronal size and tau inclusions ($r=-0.7023$; $p<0.005$); was driven by the CBD group with a negative correlation between neuronal size and tau inclusions ($r=-0.9414$; $p<0.0005$). Findings show that granule cells are smaller in the DG of 4R-FTLD-tau than those with 3R-FTLD-tau, suggesting that these species have unique pathogenic cellular profiles. Tau inclusions in CBD are related to neuronal shrinkage; contrasting with PiD where despite a high density of inclusions, neuronal size is larger. Future studies will examine proxies of neuronal integrity and tau in other neuroanatomic regions.

33. Interaction of Target Placement and Spatial Consistency During Multiple-Target Search
presented by Sarah Millross, Queen's University

When searching a scene for an object, people attend to locations where they most expect to find them. Additionally, research has shown that searching for multiple targets results in increased search times. Researchers have posited that the need to change between visual criteria (based on each target) led to the search time costs. In the current study, we will examine whether assumptions about where the target objects typically appear either helps or hinders when targets appear in either similar or different locations to one another. To examine the contribution of the location prediction, on half of the trials the targets will appear in a region inconsistent with its predicted location (i.e., on the floor instead of a countertop). If location prediction contributes to the cost of switching between multiple targets, we predict that search time will increase when a target is not in its predicted region, but the cost will be much greater when unexpected targets are in the same region. This study will lead to an increased understanding of the combined roles of target placement and spatial consistency during multiple target search, and how these factors contribute to search strategy and duration.

34. Characterizing cortical responses using fNIRS while healthy young adults perform KINARM sensorimotor tasks *presented by Cassidy Bretney, Catherine Fawzy, Celine Habashy, Chloe Hall, Erin Ford, Xianglong Chen, Queen's University*

Sensorimotor and cognitive performance assessment is important for diagnosis and rehabilitation of various neurological injuries/disorders, and the gold-standard for such assessment is the standard task battery using the KINARM Robotic device. The KINARM device has never been used in combination with functional neuroimaging to simultaneously assess brain activity and motor performance, but this could provide a good way to assess rehabilitation of function. The objective of this study is to characterize cortical responses using functional near-infrared spectroscopy (fNIRS) in healthy participants aged 18-25 during performance of the KINARM standard task battery. Participants will complete standardized sensorimotor tasks (e.g.,

visually guided reaching and reverse reaching) using the KINARM Exoskeleton while their brain activity is simultaneously recorded using NIRx NIRSport2 fNIRS. The overall objective is to characterize the magnitude and time course of frontal and motor cortical activity during sensorimotor tasks in young adults, and determine its correlation with performance. Ipsilateral and contralateral hemodynamic activity will also be characterized as a function of hand dominance within subjects and as a function of biological sex between subjects. Characterization of cortical responses to KINARM tasks will allow for the creation of a normative model of hemodynamic responses based on performance metrics like reaction time, velocity, and accuracy. Comparing KINARM task performance quartiles with average hemodynamic responses could reveal neural activity patterns which predict better performance on motor tasks. Future research can utilize this data as a comparator with impaired cortical activity and task performance. Establishing a model of the normal cortical response on standardized motor tasks is an understudied area of research that will provide a foundation for later understanding of abnormal cortical responses. Observed patterns of hemodynamic activity could someday predict specific sensorimotor deficits in patients with neurological damage, informing accurate diagnosis or targets for rehabilitation.

35. Female Long-Evans rats exhibit anhedonia-like behaviour in a two-hit model of depression-like behaviour ***presented by Irelande Farrell, Queen's University***

The limited bedding/nesting (LBN) paradigm is a naturalistic model of early-life adversity where rat dams are provided with insufficient nesting material. This alters maternal behaviour by increasing rough handling of pups and leads to long-lasting changes in behaviour and neurodevelopment of LBN offspring. However, studies examining depression-like responding in LBN offspring find inconsistent results. The current study sought to examine whether LBN renders offspring more susceptible to a "second hit" of stress in adolescence. Dams and their litters were exposed to either neonatal Control (nCON) or LBN conditions in the homecage from PD2-9. On PD21, female offspring were weaned and housed 4 rats/cage, then left undisturbed until late adolescence. In late adolescence (PD48-60), half of each neonatal group (nCON vs LBN) were randomly assigned to either the adolescent Control (aCON) or chronic mild stress (CMS) groups. CMS offspring were exposed to 2 mild stressors/day for 12 days (e.g., wet bedding exposure, 80dB white noise, restraint stress). In adulthood (>PD60), all female offspring were tested in the sucrose preference test to assess anhedonic depression-like behaviour. Female offspring in the two-hit (LBN-CMS) group displayed decreased sucrose preference relative to the three other groups, which did not differ from each other. These results are consistent with a two-hit model and suggest that a "second hit" of stress compounds the effects of LBN, inducing depression-like behaviour in LBN offspring. Ongoing work is assessing the expression of oxytocin in the paraventricular nucleus of the tested offspring, using immunohistochemistry.

36. A Literature Review: The Current Challenges in Biomarker Discovery for MDD ***presented by Isabelle Steele, Queen's University***

Introduction: Major Depressive Disorder (MDD) is a mood disorder that is characterized by significant changes in mood, accompanied by psychophysiological symptoms such as changes in sleep or appetite (Belmaker & Agam, 2008; Otte et al., 2016; Strawbridge et al., 2017). The heterogeneity of MDD has led to difficulty treating this disorder. Biomarkers, indicators of

biological processes (Mayeux, 2004), have the capacity of identifying subtypes of MDD and gaining information on effective treatment courses. This review has the goal of identifying the challenges in biomarker discovery for MDD. **Methods**: The literature encompassing past and current research pertaining to the topic of biomarkers for MDD will be examined in this investigation. Search engines like Google Scholar and Omni, Queen's University Library, will be utilized to select studies, the results narrowed down with keywords such as 'Major Depressive Disorder', 'Biomarkers', 'Challenges', and 'Discoveries'. **Anticipated Results**: It is anticipated that the large volume of potential biomarkers hinders the process of confirming which biomarker will be useful for treating MDD. This is likely the result of a lack of investigation or understanding of potential biomarkers, and determining how these biomarkers should be grouped. The heterogeneity of MDD and its treatments, as well as external variables such as medication and environmental factors, are likely to be the main challenges when searching for biomarkers of MDD. These challenges often lead to studies being non-conclusive, providing more questions than answers. **Implications**: These results lead to the conclusion that measurement challenges such as cost, time and complexity are why certain biomarkers have been researched inadequately. Identifying these challenges highlight the need for effective solutions to analyze all data within the literature of MDD, such as using big data technology. This may facilitate the grouping of biomarkers amid other variables, thus grouping subtypes of MDD in the hopes of furthering future research related to treatment of MDD.

37. Predicting Molecular Subgroups of Medulloblastoma Using Machine learning Analysis of MRIs *presented by Sawsan Haider, Queen's University*

Medulloblastoma (MB) is a malignant brain tumour originating in the cerebellum. It accounts for about 20% of childhood brain cancers. MB can be classified into four molecular subgroups: wingless (WNT), sonic hedgehog (SHH), Group 4, and Group 3, each with differing prognostic outcomes. Accurate identification of these subgroups is vital for prognosis and treatment personalization. The extent of tumour resection, for instance, impacts survival differently across subgroups, emphasizing the need for precision in MB management. Machine learning (ML), particularly convolutional neural networks (CNNs), offers potential advancements in this field. ML models, utilizing radiomic analysis of MRIs, can unveil subtle image features and provide insights into tumour characteristics. The core objective of this study is to develop an ML model to predict MB molecular subgroups using MRI radiomic features. This will involve training a CNN on a dataset of ground-truth MRI images labeled by radiologists. The model aims to investigate up to 590 radiomic features, such as tumour edge sharpness and post-contrast patterns. We will analyze T1-, T2-, and diffusion-weighted MRI images from a robust (100+) sample size sourced from various clinical centres. By incorporating various MRI modalities, the study aims to optimize pattern recognition for all MB subgroups. The secondary aim of this research is employ the model to identify potential subtypes within known subgroups. The anticipated ML model offers deeper insights into the disease's heterogeneity, driving personalized treatment strategies.

38. The "Face" of Fetal Alcohol Spectrum Disorder: Are Physical Features Predictive of Brain Injury? *presented by Kasthuri Theivendirarajah, Queen's University*

Background: Fetal Alcohol Spectrum Disorder (FASD) is a neurodevelopmental disorder primarily characterized by significant cognitive impairment and distinct physical features in

individuals prenatally exposed to alcohol. These physical features (sentinel facial features and growth restriction) have been widely utilized as a primary component of FASD assessment and diagnostic since the initial clinical characterization of FASD over 50 years ago. However, either partial or complete absence of these physical features has been reported in many individuals with a history of prenatal alcohol exposure.[1,2] Moreover, there is both weak and conflicting evidence regarding the predictive relationship between physical features and brain impairment.[3,4] Consequently, current global diagnostic guidelines have been inconsistent with respect to the inclusion of these features as required diagnostic criteria.[5-7] As such, application of these tools to the same cases has been shown to provide differing results.[8] Therefore, this study will investigate the direct relationship between physical features and cognitive impairment in individuals with FASD to elucidate the relative importance of physical features in the diagnostic process. **Methods**: A retrospective cohort analysis will be conducted using the Canadian National FASD Database, an ongoing clinical repository with over 3500 clinical records from 26 clinics across Canada.[9] Cases will be grouped by a diagnosis of FASD with or without sentinel facial features and by the presence/absence of growth restriction. The mean number of brain domains impaired for each case will be calculated and then averaged for each group. A three-way analysis of variance will be conducted between the two diagnostic groups/growth restriction and stratified by age and sex. Significant associations will be evaluated using post hoc analysis. Fisher's Exact Test will be used to further characterize specific brain domain impairment patterns among the diagnostic groups and in the presence/absence of growth restriction.

39. Future developments and stigma related to the psychology of food-related stress on the cardiovascular system in women's health ***presented by Shafagh Razaghzadeh-Shabestari, Queen's University***

Introduction: Women's health has evolved over the years, creating a stigma on the perfect meal and physiological shape, leading to psychological stress. Studies identified that different stress levels related to perceptions of meals and beverage consumption could impact the influence of hyperglycemia on baseline blood flow patterns, specifically the oscillatory shear index (OSI), in food-stress-prone women. An elevated OSI can negatively influence vascular function. Objective is to study further the impact of a high-fat meal or drink on OSI when the food is consumed under a condition designed to elicit stress. **Methods:** Twenty-five young, healthy, non-smoking women identified via questionnaire to be high in food-related stress will participate in three conditions: 1) high perceived calorie/fat/sugar (HP), 2) low perceived calorie/fat/sugar (LP), 3) and water condition (control). Brachial artery antegrade blood velocity, retrograde blood velocity, and diameter will be measured with duplex ultrasound pre-consumption and 54 minutes and 84 minutes post. Shear rate will be calculated as antegrade or retrograde velocity/diameter. **Results:** We expect the OSI before food consumption (pre) will not generally differ between the three conditions. However, post food consumption, we expect that the OSI will be greater than pre in the HP and LP conditions and greater in HP vs. the LP condition. **Conclusion:** This study will provide insight regarding the interaction between feelings about food and the physiological impact of food, specifically a potentially deleterious shear stress pattern, in food-stress-prone women and their evolution of health recommendations.

40. Understanding Variability in Rodent Middle Cerebral Artery Occlusion (MCAO) Infarct: Implications for Preclinical Stroke Research ***presented by Sapphire Newman-Fogel, Queen's University***

Middle Cerebral Artery Occlusion (MCAO) is a widely used experimental model for studying cerebral ischemia in rodents, providing insights into stroke pathophysiology and therapeutic interventions. However, variability in infarct outcomes poses challenges for data interpretation and translation to clinical settings. This study aimed to investigate the sources and implications of variability in rodent MCAO infarcts, with implications for future preclinical stroke research. The study utilized a rodent model of MCAO to assess behavioral and volumetric deficits following stroke induction. Results revealed significant heterogeneity in infarct size and extent, influenced by factors such as individual vascular anatomy, surgical techniques, and experimental methodologies. Variability in stroke induction techniques and outcome measures underscored the need for standardized protocols and rigorous quality control measures in preclinical stroke research. Key findings include the need for larger sample sizes to account for variability in stroke outcomes, optimization of surgical techniques to improve reproducibility, and incorporation of advanced imaging modalities for comprehensive assessment of stroke. Multimodal outcome measures, including behavioral testing and histological analysis, were recommended to provide a comprehensive evaluation of stroke outcomes. The study highlighted the translational challenges associated with variability in preclinical stroke models and emphasized the importance of collaboration between researchers, clinicians, and industry partners to address these challenges. By implementing modifications to trial design and methodology, researchers can enhance the reliability and reproducibility of preclinical stroke models, ultimately advancing our understanding of stroke pathophysiology and facilitating the development of novel therapeutic interventions for stroke patients.

Student Oral Presentation Abstracts

1. **Exploring oculomotor biomarkers for neurodegenerative disease diagnosis and features using structured and unstructured eye movement tasks** ***presented by Heidi Riek, Queen's University***

Developing behavioural markers for neurodegenerative disease will prove a significant advancement in their diagnosis. Due to extensive overlap between oculomotor and neurodegeneration-affected circuitry, quantifying saccade behaviour produces many objective potential biomarkers for neurodegenerative diseases. Both structured and unstructured tasks yield parameters that comprehensively characterize saccade behaviour, but understanding links between task parameters and their relationships to disease processes is crucial to use of eye movements as the foundation of future disease screening and diagnostic tools. We evaluated saccade behaviour in a large cohort of patients from the Ontario Neurodegenerative Disease Research Initiative: 30 Alzheimer's disease, 72 mild cognitive impairment, 9 progressive supranuclear palsy (PSP), and 119 Parkinson's disease, and 104 healthy age-matched controls. All completed a structured task (interleaved pro- and anti-saccade task (IPAST): looking at or away from a peripheral visual stimulus according to the colour of a central fixation point) and an unstructured task (free viewing task (FV): instruction-free viewing of rapidly switching video clips). Examination of differences between disease groups in each task revealed that both can differentiate diagnoses and disease features. IPAST revealed increases in anti-saccade error rates (indicating voluntary control deficits) with cognitive impairment, and motor impairment (e.g. saccade hypometria) in movement disorders, but few limitations in fast visuomotor processing. FV revealed key disease features such as vertical gaze impairment in PSP and between-group saccade rate differences immediately following clip change-induced visual perturbation. Inter-task correlations may illuminate shared underlying neural circuitry; preliminary results suggest parameters from early epochs following FV clip change correlate to fast visuomotor parameters from IPAST, while saccade rate in later epochs correlates to IPAST parameters measuring voluntary control. Full behavioural characterization of structured and unstructured oculomotor tasks in neurodegeneration, and links between tasks, will enable development of an objective behaviour-based clinical screening tool leveraging the breadth of oculomotor data to diagnose neurodegenerative disease.

2. **Relevance of sex as a biological variable in assessing the efficacy of a gene replacement therapy for a mouse model of XLID98** ***presented by Eve Racette, Queen's University***

Five to ten percent of intellectual disability (ID) cases in males are linked to mutations of various genes located on the X chromosome, one of which is the Neurite Extension and Migration Factor gene (*NEXMIF*). The loss of NEXMIF causes X-Linked Intellectual Developmental Disorder 98 (XLID98), a syndrome characterised by intellectual disability, autism spectrum disorders and drug-resistant epilepsy. While the role of NEXMIF is poorly understood, studies have suggested its involvement in neurite outgrowth and orientation, in neuronal migration and in gene expression. Previous studies of the role of Nexmif in rodents have only been carried out in males, limiting the relevance of these models for the assessment of future gene therapy. Our hypothesis is that the loss of Nexmif causes a variety of neuronal phenotypes due to the alteration of neurodevelopmental processes, such as motility, neurite growth, synaptic formation, gene expression, etc. To verify this hypothesis, we assessed **a)** cognitive impairments using behavioural assays, **b)** hippocampal network excitability and short term facilitation using *ex vivo*

local field potential recordings and **c)** gene expression alterations in the brain using MicroArrays. Similar to what is observed in XLID98 patients, loss of Nexmif is associated with sex-specific phenotypes in mice. Affected females are hyperactive in the Open Field test and their hippocampal network activity is decreased as compared to age-matched controls. Affected males are hypoactive in the Marble Burying test, indicative of a lack of interest for the external environment, have hyperactive hippocampal networks and display abnormal gene expression patterns. Interestingly, males also present with adult-onset obesity and frequent seizures. Our data suggests that, like in humans, XLID98 is associated with a variety of sex-specific phenotypes, further reinforcing the relevance of assessing both sexes in the development of gene replacement therapy for this disorder.

3. **The impact of a murine coronavirus upon alpha-synuclein pathology in neurons and microglia** *presented by Stephanie Hobbs, Carleton University*

Parkinson's Disease (PD) is characterized by a loss of midbrain dopamine neurons and the accumulation of aggregates of oligomeric and fibril forms of the alpha-synuclein protein. The multi-hit hypothesis points to an interaction between genetic and multiple environmental risk factors in the cause of the disease (Ball et al. 2019; Srinivasan et al. 2021). Much evidence has indicated that mutations in the inflammatory leucine rich repeat 2 (LRRK2) protein is critically linked to PD (Cabezudo et al. 2020). Moreover, viral infection may play a role as an environmental trigger and may do so by augmenting the pro-inflammatory consequences of LRRK2. The present study utilized primary midbrain microglia and neurons from wildtype and LRRK2-G2019S mutant mice. Murine Hepatitis Virus (MHV) was utilized as a model for coronavirus infection and real-time live cell imaging and immunobiological assessments used to assess changes in microglial morphology, microglia-neuron interactions and alpha-synuclein aggregation in response to MHV. Thus far, we have found that MHV robustly infects midbrain dopamine neurons and microglia, leading to time-dependent neurodegeneration. The virus also caused microglial activation, increased motility and resulted in cell fusion with the formation of complex syncytia networks. These effects were generally increased in the LRRK2 G2019S derived cells and the mutation appeared to catalyze the spread of alpha-synuclein. Our preliminary data indicate an importance for microglia and LRRK2 in coronaviral neurotoxicity and alpha-synucleinopathy, which has tremendous clinical implications.

4. **The Dynamic Synchronization of Brain and Thought** *presented by Raven Wallace, Queen's University*

The contextual relevance of our external environment significantly influences our thoughts (Mulholland et al., 2023), but measuring thoughts is hindered by the complexity of assessing mental states compared to objective indicators of cognition, such as fMRI (Turnbull et al., 2019). My research assesses the relationship between common timecourses within the brain and thoughts under naturalistic stimuli using multi-dimensional experience sampling (mDES), a reliable tool for estimating thought patterns sensitive to experiential changes, to assess how thought synchrony occurs during movie watching and how this is represented in the brain (Smallwood et al., 2016). Using a unique sampling technique, lab participants respond to mDES probes during three movie clips, which described movie-watching into patterns of thought defined as "Past Knowledge," "Intrusive Distracting," "Unpleasant Detailed-Focus," and "Sensory Engagement." I found different thought patterns for each movie genre and generated experiential

time courses across each movie to identify how thought patterns vary over time. Using OpenfMRI data, I identify how the activation of neural networks in participants who watched the same film in the scanner synchronizes with the lab sample's experiential time course (Aliko et al., 2020). Across the whole brain, the visual system, auditory system and motor cortex dominate the majority of neural activation—emphasizing the significance of the sensory systems during movie-watching. Lastly, I assessed how reported thought patterns might predict comprehension across lab participants and found two main effects of positive and negative overall performance and a movie-specific interaction. My analysis supports the coupling hypothesis that individuals who perform better on comprehension experience "Sensory Engagement" thought patterns, which were associated with activation in the sensory cortex. My research provides a novel method of collecting experience sampling within the laboratory during movie watching and identifies particular regions in the brain that are undoubtedly important for thought synchronization, such as the sensory systems.

5. **Bridging the gap: ghrelin and the effects of social stress on male and female mice** *presented by Brenna MacAulay, Carleton University*

Stress, a common risk factor for depression & anxiety, disproportionately affects females. Existing social stress models predominantly involve males, prompting the emergence of a novel paradigm, chronic non-discriminatory social defeat (NDSD). NDSD, derived from classic social defeat stress, induces comparable stress effects in male & female mice. In this project, we sought to determine the neuroendocrine effects of acute NDSD on male and female wildtypes (WT) and mice with mutations to the ghrelin receptor (GHSR KO). GHSR is a 7-TM receptor found in stress-related brain regions. Genetic manipulation of GHSR influences metabolic, cellular, & behavioural responses to stress in males. To test this, male/female pairs were added to the cage of a male CD-1 mouse for 10 min. The CD-1 aggresses towards both intruders. They were then separated and sacrificed. Groups were chosen by genotype, estrus cycle phase, and sex. As expected, acute NDSD led to increased plasma corticosterone and ghrelin levels compared to all non-stress controls. Notably, stressed WT and KO males showed higher corticosterone levels than all females. Using cFos as a marker for neuronal activation, we found stress increased paraventricular nucleus (PVN) activation in all groups. In females, KO mice sacrificed pre-ovulation showed a higher cellular response to stress than WT counterparts, but not those sacrificed after. Stressed mice, regardless of sex, displayed higher cFos expression in the arcuate nucleus, but all females showed higher cFos density than males in both groups. This data highlights a differed response to an acute social stressor in males and females, suggesting that in the female PVN, stress-induced activation is moderated by the GHSR and potentially estrogen.

6. **Analyzing the Relationship Between Altered Descending Pain Regulation in Fibromyalgia Syndrome (FM) and its Connection to Autonomic Dysregulation: A Comprehensive Structural and Physiological Modeling (SAPM) Study Using Functional MRI Data** *presented by Shima Hassanpour, Queen's University*

Fibromyalgia (FM) is a chronic pain condition that affects a significant portion of the population. Despite its severe impact on daily functioning and overall well-being, FM is still poorly understood. Prior research has suggested that individuals with FM display heightened sensitivity to pain and signs of autonomic dysfunction. Therefore, this study aimed to identify altered neural processes underlying pain sensitivity in FM using fMRI of the brainstem and spinal cord. Pain regulation in the brainstem and spinal cord involves reactive and continuous components that occur before, during, and after applying a noxious stimulus. Evidence to date

indicates that functional differences in FM are mainly in brain regions associated with motivating elements of pain processing, and essential differences in nociceptive processing in brainstem and spinal cord regions have also been identified. We hypothesized that nociceptive processing is altered in FM compared to HC in areas of the brainstem and spinal cord that are involved in autonomic regulation and descending pain regulation, including the parabrachial nuclei (PBN) and nucleus tractus solitarius (NTS). Existing fMRI data from the BS and SC were used from previous studies in our lab involving 30 female participants (15 FM and 15 HC). Data were obtained while a calibrated noxious heat stimulus was applied to the palm of the right hand (C6 dermatome) before and after the push. Participants were trained to rate their pain and were familiarized with the stimulation paradigm. They knew when to expect the trigger and could "anticipate" the discomfort. fMRI data were analyzed using Structural and Physiological Modelling (SAPM), a novel connectivity analysis method developed in our lab. The SAPM method provides a model of neural signaling that explains observed BOLD signal characteristics and includes information about inhibitory and excitatory signaling. SAPM results demonstrate significant brainstem/spinal cord connectivity differences between the FM and healthy control groups. The regions involved in these differences in connectivity included the locus coeruleus (LC), thalamus, NTS, PBN, and right dorsal part of the spinal cord in the C6 segment. The results reflect inhibitory and excitatory signaling differences likely in controlling arousal and autonomic homeostatic regulation. This provides possible evidence that women with FM have altered pain modulation compared to healthy controls.

7. Timing of eye and hand movements during reaching depends on functional demands of gaze *presented by Nethmi Illamperuma, Queen's University*

When reaching to visual targets, people are unable to shift their gaze away from the reach target to a secondary gaze target until after the reach target has been attained—a phenomenon known as gaze anchoring. Here, we compared gaze anchoring when reaching to a visual target versus a visual-haptic target providing force feedback upon contact. We also examined gaze anchoring in a bimanual context in which participants were instructed to shift their gaze to the secondary target as soon as it appeared and, at the same time, move their other hand to the secondary target. In our task, human participants (n=28) used their right hand to move the handle of a robotic manipulandum to a primary visual or visual-haptic reach target. A secondary target was present at the beginning, halfway, or end of the reaching movement and participants were instructed to make either an eye movement (unimanual trials) or a combined eye and left hand movement (bimanual trials) to this target as soon as it appeared. We found that in unimanual trials with visual targets, saccades were initiated ~125 ms after the hand cursor 'visually contacted' the reach target. In contrast, with visual-haptic targets, saccades were initiated around the time of contact. This suggests that when haptic feedback was provided, central vision was not critical for guiding the hand as it approached the target or checking target attainment. However, gaze anchoring was still observed with visual-haptic targets earlier in the reach when gaze was engaged in directing the hand towards the target. In bimanual trials, gaze anchoring was observed but anchoring did not extend to the left hand, the onset of which was decoupled from gaze. Overall, our findings indicate that the timing of eye and hand movements in object manipulation is linked to the function of target fixations.

8. Hydrogen peroxide and phosphotyrosine modulate voltage-dependent cation channels *presented by Emily Robichaud, Queen's University*

Reactive oxygen species (ROS), such as hydrogen peroxide, are produced during mitochondrial oxidative metabolism. (Hancock et al, 2001) H2O2 production has been established as a key biochemical event in many cell signaling pathways and is linked to

phosphorylative processes. (Sies, 2017, Hancock et al, 2001) Cation channel modulation contributes to long-term changes in excitability in *Aplysia Californica b*ag cell neurons, which exhibit prolonged firing when exposed to certain stimuli. Cholinergic input initiates the aPerdischarge to trigger events, releasing the egg-laying hormone into the bloodstream and culminating in the deposition of an egg mass. During this process, the mitochondria produce H2O2 by electrons leaking from the electron transport chain. (Wong et al, 2017) This research uses whole-cell recording, an electrophysiological technique which measures current responses. Prior research has shown the ability of bath-applied H2O2 to produce inward currents in bag cell neurons specific to cation channels. Furthermore, phosphotyrosine levels are reduced in the presence of H2O2. This suggests that H2O2 and tyrosine phosphorylation interact in some manner to keep cation channels open and maintain the aPer-discharge firing rates. This paper aims to better characterize the observed reduction in phosphotyrosine levels in the presence of mitochondrial H2O2 and the subsequent effect on neuronal firing rates. Preliminary results indicate that tyrosine kinase inhibitors produce an inward current comparable to that produced by H2O2. Preliminary data further suggests these effects may occlude one another, though further investigation is required.